REMARKS

The Office Action mailed March 27, 2003 (Paper No. 10) has been carefully reviewed and the foregoing amendments are made in response thereto. In view of the amendments and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Applicants respectfully submit that no prohibited new matter has been introduced by the amendment. Support for the amendment to the claims can be found throughout the specification and claims as originally filed, for example at page 2, lines 30-33. Entry of the amendment is respectfully requested.

Status of the Claims

Upon entry of the foregoing amendment, claims 1-11 will be pending.

Information Disclosure Statement

Applicants filed with this application a PTO form 1449 citing 13 references on November 28, 2001. A copy of the date-stamped return receipt post card indicating the same is enclosed. A signed, initialed and dated copy of the PTO form 1449 indicating that the Examiner has considered each of the listed references was not received with the Office Action mailed March 27, 2003. Accordingly, Applicants enclose herewith a copy of the PTO form 1449 filed on November 28, 2001 along with copies of each of the references listed thereon. Applicants respectfully request that the Examiner consider each of the listed references and indicate the same by signing, dating, initialing and returning the enclosed PTO form 1449 to Applicants. No fees are believed due with respect to this submission.

The Rejection of Claims 1-8 Under 35 U.S.C. § 112 First Paragraph

Claims 1-8 stand rejected under 35 U.S.C. § 112 first paragraph because it is alleged that the specification does not provide enablement for "applying a voltage of not more than 50 volts to any kinds of cells without any given duration of pulse..." Office Action at page 2. Applicants respectfully traverse the rejection for the following reasons.

The pending claims have been amended to recite "applying a continuous voltage of not more than 50 volts..." Applicants assert that it would not require undue experimentation for a person skilled in the art to practice the claimed invention because the claims require that a continuous voltage of not more than 50 volts be applied.

Applicants submit that no experimentation would be required to practice the claimed invention because, rather than using "pulses" of "any given duration" as alleged in the Office Action at pages 2 and 3, the claims require that the applied voltage be continuous. Thus, a person skilled in the art would know how to practice the claimed invention without undue experimentation because the claims recite how to practice the methods.

The Office Action alleges that "the results of experiments involving applying a voltage of not more than 50 volts to any kinds of cells without specifying the durations of pulses is not predictable." Office Action at page 4. Applicants respectfully disagree. As stated above, the applied voltage is continuous. The specification at page 2, lines 17 to 21 explains that "[i]t has now been found that it is possible to obtain release of intracellular material from cells by the application of voltages of lower order magnitude not previously thought to be capable of affecting cell membrane structure in such a way." The specification at page 2, lines 3 to 12 explains further that this finding is in contrast to known electroporation methods using voltages in the kilovolt range and pulses of short duration on the order of milliseconds. Thus, Applicants respectfully submit that the claims, as amended, are fully enabled by the specification because the claims recite the steps necessary to practice the claimed methods. Withdrawal of the rejection is respectfully requested.

The Rejection of Claim 12 Under 35 U.S.C. § 112 Second Paragraph

Claim 12 stands rejected under 35 U.S.C. § 112 second paragraph for allegedly being indefinite. Without acquiescing to the grounds of the rejection and solely to expedite prosecution, Applicants have cancelled claim 12. Withdrawal of the rejection is requested.

The Rejection of Claims 1-12 Under 35 U.S.C. § 103(a)

Claims 1-12 stand rejected under 35 U.S.C. § 103(a) for allegedly being unpatentable over U.S. Patent 5,186,800 to Dower. Applicants respectfully traverse the rejection because the

Office Action fails to make a *prima facie* case against the claims and it relies on improper hindsight in filling the gaps acknowledged by the Office to exist in the cited reference.

The Office Action states, at page 7, second paragraph, that "Dower does not disclose applying the voltage not more than 50 volts [sic] including the range of the voltage between 0.5-50 volts, the spacing between two electrodes is no more than 5mm or 10mm and the period for applying voltage is at least 30 seconds or 2 minutes continuously."

The Office Action acknowledges that the claimed limitations are not taught in the Dower patent and provides no indication of where the limitations are taught. Instead, the Office Action states that one of ordinary skill in the art would arrive at the claimed invention by "optimization of the amount of volts, the space between two electrodes and the time needed for the pulse." Office Action at page 7, paragraph 3.

Because the Office Action lacks a teaching or suggestion in any reference of the limitations present in the claims, Applicants respectfully submit that a *prima facie* case of obviousness has not been made against the claims.

The M.P.E.P. at 2143 lists the three basic requirements of a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations [emphasis added].

Applicants submit that since the Office acknowledges that Dower does not teach the limitations present in the claims and provides no indication of where these limitations are taught, a *prima facie* case of obviousness has not been made. Furthermore, Applicants respectfully assert that it is improper hindsight to use Applicants' own disclosure to fill the gaps acknowledged to exist in the cited reference to construct an obviousness rejection. Withdrawal of the rejection is requested.

Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of all outstanding rejections and early notice of allowance to that effect. Should the Examiner believe

that a telephonic interview would expedite prosecution and allowance of this application, she is encouraged to contact the undersigned at her convenience.

Applicants believe that no fees are required with this filing, however, except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No.50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

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